

Attorney Docket No.: ISPH-0500  
Inventors: Yu et al.  
Serial No.: 09/705,587  
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In the Claims:

Please amend the claims as follows:

DL 13. (amended) A method for detecting an antisense oligonucleotide 20 to 30 nucleobases in length in a bodily fluid or extract at concentrations between about 50 picomolar and 1400 picomolar, consisting of the steps of:

a) contacting a liquid sample with a probe complementary to an antisense oligonucleotide that is 20 to 30 nucleobases in length so that the probe and the oligonucleotide can form hybrid moieties in said liquid sample, wherein said probe comprises a detectable marker and a binding moiety and said detectable marker and said binding moiety are covalently bound to said probe;

b) placing said liquid sample in contact with a solid support to which a binding partner of said binding moiety is attached so that said hybrid moieties present in said liquid sample will be attached to said solid support, and wherein said binding partner's ability to detect said antisense oligonucleotide is independent of the sequence of said oligonucleotide;

c) removing any oligonucleotide from said liquid sample that has not formed a hybrid moiety;

d) contacting said liquid sample with a single strand oligonucleotide-specific nuclease under conditions in which probe

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D/ which is not hybridized to form said hybrid moieties is degraded and thus is no longer attached to said solid support;

e) removing any unbound detectable marker from said liquid sample; and

f) detecting a label associated with said marker wherein the presence of said label indicates the presence of said hybrid moieties bound to said solid support wherein detection of said label at levels above the level characteristic of a liquid sample that was prepared as a blank sample to contain no antisense oligonucleotide indicates the presence of said antisense oligonucleotide in said liquid sample at concentrations between about 50 picomolar and 1400 picomolar.

D/ 15. (amended) The method of claims 13, wherein said antisense oligonucleotide comprises at least one phosphorothioate linkage.

16. (amended) The method of claim 13, wherein said antisense oligonucleotide comprises a modification at the 2' position of at least one sugar moiety.

D/ 18. (amended) The method of claim 13, wherein said antisense oligonucleotide comprises at least one modified base.

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#### REMARKS

At the outset, Applicants thank the Examiner for the courtesy of the telephone interview on November 20, 2002. Claims 13-22 are pending in the instant application. Claims 13-22 have been rejected. Claims 13, 15, 16 and 18 have been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### I. Rejection of Claims Under 35 U.S.C. 102(e)

Claims 13 and 21 have been rejected under 35 U.S.C. 102(e) as being anticipated by Impraime et al. (US Patent 6,228,578). The Examiner suggests that this reference teaches a method for detecting an oligonucleotide in a body fluid by preparing a bodily fluid, contacting the fluid with a probe complementary to the oligonucleotide wherein the probe comprises a detectable marker and a binding moiety, placing the fluid in contact with a solid support to which the binding partner is attached, removing any oligonucleotide from the sample that has not formed a hybrid moiety, contacting the fluid with a single strand specific nuclease to degrade non-hybridized oligonucleotides and detecting a label